Prediction of Non-Alcoholic Fatty Liver Disease Stages Through CT-Scan And Sonography Using Neural Network

MSc Research Project
Data Analytics

Souvik Maitra
Student ID: x20194617

School of Computing
National College of Ireland

Supervisor: Mr.Prashanth Nayak

National College of Ireland
Project Submission Sheet
School of Computing

Student Name:	Souvik Maitra
Student ID:	x20194617
Programme:	Data Analytics
Year:	2022
Module:	MSc Research Project
Supervisor:	Mr.Prashanth Nayak
Submission Due Date:	15/08/2022
Project Title:	Prediction of Non-Alcoholic Fatty Liver Disease Stages Through CT-Scan And Sonography Using Neural Network
Word Count:	7851
Page Count:	27

I hereby certify that the information contained in this (my submission) is information pertaining to research I conducted for this project. All information other than my own contribution will be fully referenced and listed in the relevant bibliography section at the rear of the project.

ALL internet material must be referenced in the bibliography section. Students are required to use the Referencing Standard specified in the report template. To use other author's written or electronic work is illegal (plagiarism) and may result in disciplinary action.

Signature:	
Date:	17th September 2022

PLEASE READ THE FOLLOWING INSTRUCTIONS AND CHECKLIST:

Attach a completed copy of this sheet to each project (including multiple copies).	☐
Attach a Moodle submission receipt of the online project submission, to each project (including multiple copies).	☐
You must ensure that you retain a HARD COPY of the project, both for your own reference and in case a project is lost or mislaid. It is not sufficient to keep a copy on computer.	☐

Assignments that are submitted to the Programme Coordinator office must be placed into the assignment box located outside the office.

Office Use Only	
Signature:	
Date:	
Penalty Applied (if applicable):	

Prediction of Non-Alcoholic Fatty Liver Disease Stages Through CT-Scan And Sonography Using Neural Network

Souvik Maitra
x20194617

1 Abstract

Cirrhosis which is the last and fourth stage of NAFLD caused in the liver is one of the major diseases of concern in the world with cases rising every year.Fatty liver diseases such as non-alcoholic fatty liver diseases (NAFLD) generally don't cause many problems for the patients as such but it does have the possibility to progress into a more dangerous disease of Liver Cirrhosis. Identification of such progression beforehand can be very beneficial for the patients as well as the doctors.For the patients, it can save their lives as well as money that may be required for screening and operations.Doctors can make use of this information to direct the treatment in the proper direction to help patients.Hence a system for early detection of fatty liver disease into liver cirrhosis is a need in modern medicine healthcare infrastructure. This research has been focused on the early detection of the disease.The study implemented four distinct models of machine learning for predictions viz.Recurrent Neural Network, Deep Recurrent Neural Network, Support Vector Machines, and Random Forest.Our proposed research method is superior at identifying the stages using the Deep Neural Network with balanced accuracy of 96.7%.

2 Introduction

In the human body, the liver is one of the most important organs that support the proper operation of different biological and metabolic activities.The liver plays a vital and important role in the human body to regulate different chemical activities or processes such as metabolism, storage, and secretion.In this process, it has also been observed that the liver works as the primary organ in the human body to convert as well as detox different toxic substances into non-toxic substances.Along with that, this vital organ also supports in excretion of waste materials from the human body as well. Besides liver also produces bile, an essential body fluid, which is the primal ingredient to break down the fat intake from the food and hence regulates the digestion process.Apart from that, this powerful organ is also helpful in producing and secreting essential clotting factors in the human body. Liver plays a crucial role to store iron which helps in the production of red blood cells in the body.Further, the liver is also helpful to support the metabolic medicinal functions in the human body and operate accordingly.Thus,considering the contribution of the liver to different essential functions of the human body it can be considered a crucial organ that helps a person to live a healthy life.

However,it required to be taken good care as it may get affected by certain life-threatening chronic diseases as well.Even in the absence of proper treatment and care at the initial stage,it may cost the life of a person as well.In this process,different factors such as over-consumption of alcohol, obesity, and hepatitis infection, have been identified to cause chronic liver diseases in the human body. Without proper examination and diagnosis at the initial stage, these factors may cause severe health issues and even take the life of a person. Based on the types and reasons different liver diseases could be identified, which are- liver fibrosis, cirrhosis,fatty liver, non-alcoholic fatty liver (NAFLD),and others.According to Younossi et al. (2019), nearly 25% of the global population is presently suffering from NAFLD and it has emerged as one of the key reasons for chronic liver disease in the world. This growth or emergence of NAFLD mainly resulted due to its prevalence, complex nature of pathogenesis, difficulties faced in the diagnosis process, and lack of availability of approved therapies.Even certain studies are showing that NAFLD could emerge as the major form of chronic liver disease in children and adults and due to that, it might become the leading factor for liver transplantation as well (Neuschwander-Tetri (2017)).
Witnessing the impact and growth in the occurrence of NAFLD a higher focus has been made by the researchers to develop proper diagnosing and examining processes as well.In this process, over time different non-invasive and invasive both types of techniques and methods have been developed that could support examining and diagnosing NAFLD.In the case of invasive tests, it is required for the practitioners to cut certain body parts from where medical instruments could be inserted for performing the required tests. On the other hand, in the case of non-invasive tests,it is not required for the practitioners to cut the body parts to insert medical instruments and over the past decade, significant growth in alternative strategies such as transient elastography (TE) could be identified for NAFLD patients.Apart from that, growth in the use of the FIB-4 and NAFLD fibrosis scores can be identified as these are identified to be validated non-invasive tests available for NAFLD patients.
The major contributions of this research study are:

- It explores the success and effectiveness of neural networks to predict the progression of NAFLD into more severe complications such as cirrhosis.
- This study involves implementing Deep Recurrent Neural (DRNN) Networks for predicting the prognosis of the disease which is a novel approach in the field.
- The study also compares the results of DRNN with other conventional classification models such as Support Vector Machines (SVM), Recurrent Neural Network (RNN),and Random Forest(RF) for predicting the prognosis of NAFLD.

The rest of the report is organised as follows:-
Subsequent chapter 3 discusses the motivation for undertaking this study. Chapter 4 lists the objectives that are aimed to achieve during this study. Research questions that need to be answered using this study are listed in section 5.This is followed by chapter 6 that involves the review of literature necessary for the study.The methodology that is followed for the study is discussed in chapter 7 followed by the results and evaluation of the experimentation in chapter 8.Finally chapter 9 concludes the study with the discussion of avenues for future work.

3 Motivation

Considering the current situation and available diagnosis practices it could be identified that there is a gap present in the process of analyzing the effectiveness of existing practices for treating NAFLD.The growing trend of using non-invasive methods for treating NAFLD motivated the research work to study and evaluate the section of non-invasive where different stages of the NAFLD patients could be studied appropriately and effectively.Apart from that, this study will be performed based on pathological and hematological threshold parameters of the CT scan and Ultrasonography.Based on the findings proper decisions would be undertaken for developing a proper understanding of whether a patient consists more or less a chance of getting into the next stage of NAFLD. Apart from that, it is needed to highlight that through the completion of this research paper it is expected that more pro-active measures for a certain patient could be undertaken that can support in delivering a proper diagnosis to the patient and save his/her life as well. In the process of delivering proper treatment in NAFLD,it has been observed that a higher level of accuracy in the classification is necessary or holds utmost importance through which the desired results could be achieved.Thus, consideration of such an approach in this research paper is expected to be effective in enhancing the level of accuracy in classification for such procedures of diagnosis as it would support attaining proactive measures by the physicians for a certain patient as well.Thus,this research study is not only focused to deliver a higher benefit for NAFLD patients but also could be effective for the practitioners as well.

4 Objective

Important objectives that need to be achieved during this study are:
- To develop or build a multi-class model for diagnosing the different stages of NAFLD depending on the hematological parameters through the utilization of a deep recurrent neural network.
- To evaluate the effectiveness in making decisions that can support determining whether a patient holds a more or lower chance of getting into the next stage of NAFLD or not.

5 Research Question

This is because with the proper formulation and implication of the research question a researcher as well as the targeted audience could effectively identify the exact answer an entire research paper has focused on achieving.Taking into account the importance of a research question,for this research paper,the key research question could be identified as follows-
How precisely and constructively neural network model will help in the prediction of different stages of non-alcoholic fatty liver disease based on the haematological or pathological parameters?
To what extent the hematological features will be useful in the prediction of NAFLD progress?Can an assistive algorithm to detect NAFLD progression be developed using machine learning technologies?
.Thus, based on the identified research question it can be clearly stated that it will not only support the practitioners to identify the effective implications of the neural network

model in the determination of the stages of NAFLD but also deliver a proper means for the patients as well to acquire an effective treatment and diagnosis throughout the process.

6 Literature Review

6.1 Introduction

With the change in lifestyle and pattern of diseases, it has become a concerning factor for health practitioners as well as for the entire population of the world.In this process, it has been observed that different chronic diseases, such as hepatitis,fatty liver,non-alcoholic fatty liver disease and others,affected the proper functioning of the liver and also caused severe health issues for people as well.Even in certain cases, the lack of proper treatment and diagnosis facilities becomes life-threatening for people in case of chronic liver diseases.Over the decade a significant growth in non-alcoholic fatty liver disease has emerged as one of the key factors leading to the liver transplant for the people.Even the researchers are fearing that it could become one of the key chronic liver diseases for adults as well as children.Considering the severeness of this disease and the lack of research relating to the effectiveness of the incorporation of non-invasive treatment procedures this section of the research paper will focus on assessing the previous studies performed in this research area.This evaluation of the previous research will help to develop a proper idea relating to the focused research area in an appropriate and effective manner.

6.2 Role performed by Neural Network based model in Healthcare Domain

The present world is revolving around data and this extensive use of data has revolutionized the information technology system as it supports organizations or businesses to grow rapidly and extensively in different aspects of operations.Not only in the information technology aspect,but data has also emerged as a crucial factor in different sectors all over the world and supports businesses to expand their level of efficiency or operational effectiveness effectively and efficiently. In a study,Castera (2018) has highlighted that data evaluation holds the utmost importance for any industry or sector,like the health care sector,to enhance their operations extensively and the importance of the scene is highly crucial for sectors that are highly dominated by data. In this process,over the years a growing implication of data could be identified in the health care sector as well.This is because in the healthcare industry different relevant data are acquired and used over the period to formulate effective decisions or predictions that could support the overall care delivery system to the patients.In the 21st century, modern technologies are developed which a data-driven companies even consider these data to play a crucial role in their growth and operational process. Similarly in the healthcare sector over the past few years,different healthcare data are being used to identify the key trend and anticipate the potential impacts of certain activities on the overall service delivery system. In the healthcare system,it is essential to analyse investigate and inspect key data based on which the diagnosis and overall detection of the diseases could be performed in an effective and efficient manner.According to Neuschwander-Tetri (2017) proper implication of data-driven strategies or methods is supporting to predict and treat crucial healthcare issues like NAFLD. From a study performed byTang et al. (2019),it could be identified that Structural health monitoring or SHM is being currently used throughout the world for managing and maintaining different civil infrastructures.This is because with the proper implication of SHM systems huge amounts of data could be produced along with monitoring, mining and utilization of the same in any crucial studies. In this study,the researchers focused on detecting anomalies in the data pre-processing stage.Based on the findings of the study it could be identified that the proper implication of a novel data anomaly detection method depending on a convolutional neural network (CNN) could be effective for human vision and decision making.Thus, these data-driven models could also be identified to be utilised in different aspects of the healthcare sector and could be effective to deliver effective results to the users of the same. Even in another study Choi et al. (2017) mainly focused on exploring whether the implication of deep learning to model temporal relations among events in electronic health records would be effective to improve the performance of the model in predicting the initial diagnosis of heart failure compared to the conventional methods that do not take into account the temporality.In order to analyse the same data were acquired from a health system's EHR on more than 3800 incident HF cases and 28,903 controls.In this process, it is needed to highlight that recurrent neural network or RNN models utilizing the gated recurrent units were incorporated to identify relations among time-stamped events consisting of cases and controls of a time-frame of 12-18 months.Based on the area under the curve for the RNN model was 0.777 compared to AUCs for logistics regression at 0.747.Depending on the findings the researchers concluded that the models of deep learning must be incorporated for better performance of models for detection of incident heart failure which consists of a time window of 12-18 months.

Alkhatib (2022) highlighted in a study that as there are diverse liver illnesses present and hence different liver function tests,like alanine transaminase (ALT) could be used to diagnose them.This study particularly focused on implementing a neural network analysis process to forecast liver disease and also to identify the relative contribution of various liver disease predictors as well.A Kaggle data set was used by over 583 people to study the same. In the prediction model different predictors were used,such as ALT, albumin/globulin ratio,age,gender and others and in 79.6% of cases the concerned model was successful to make a proper prediction.In this regard, ALT emerged as the most key predictor to consider and hence in the overall aspect neural network analysis model is observed to be effective to predict liver illness from one perspective.Sharma et al. (2022) mainly focused on their study to highlight the implication of different machine learning approaches or models such as Random forest, ridge, logistic regression,SVM,neural network and others, to identify whether these could be used to classify different cardiovascular disease in patients who are suffering from nonalcoholic fatty liver disease in the UK.In this process, based on the findings it could be stated that the implication of a machine learning algorithm could be effective that supports in identifying CVD in patients who are suffering from NAFLD through the proper integration of appropriate lifestyle, clinical and genetic research factors.This is because the implication of such a technique would be effective to identify the patients with NAFLD at higher risk of CVD and those patients would be provided with the treatment of their cardio-metabolic risk factors to restrict the occurrence of any cardiovascular mortality.

Sorino et al. (2021) Recognized in their study that NAFLD Creates an adverse impact on nearly 20 to 30% of the adult population in different developed countries.The research particularly focused on developing and validating a simple neural network-based web application that could be utilized in predicting NAFLD,particularly its absence.In this process, the researchers focused on verifying the accuracy percentage, confusion matrix, negative predicted value or NPV values,the area under the ROC curve,precision,f1 score and others.The researchers highlighted from the findings that the neural network was successful in achieving a 77% accuracy level at the time of testing and at that time the area under the ROC curve was valued at 0.82.Hence,considering these findings the focused approach would be effective to support the NAFLD diagnosis and minimise the costs of healthcare.

6.3 Ultrasound and CT scan utilizing Neural Network Model

Chen et al. (2017) highlighted in a study that ultrasound imaging is significantly used as a screening tool for obstetric evaluation and diagnosis.In this process, it has been identified that the researchers were focused on forming a general framework for the automatic detection of different standard planes from US videos.Based on the findings it could be identified that the novel composite framework of the convolutional and recurrent neural networks delivered better and more accurate results compared to the conventional one.In this aspect,Lupsor-Platon et al. (2021) mainly focused on discussing and identifying the performance of the ultrasonography technique in NAFLD and related hepatocellular carcinoma treatment and diagnosis.Along with that it also focused on assessing the role of AI-based methods,specifically the implication of the deep learning algorithms to improve the quality of the image processing of liver ultrasonography.The findings show that in spite of certain limitations the use of deep learning algorithms could be effective for assessing the NAFLD and NAFLD-related HCC and also delivering a better treatment or diagnosis over time as well.

Van Kleef et al. (2022) recognized in a study that the burden of NAFLD is increasing significantly due to the growth of the obesity situation. In this process, the researchers have focused on performing a cross-sectional analysis targeting a certain population in the Rotterdam study cohort.In this process, data were acquired based on abdominal ultrasound and accelerometry which was performed between 2009 and 2014.In the absence of secondary reasons or causes for steatosis, such as steatogenic drugs,viral hepatitis and over-consumption of alcohol,NAFLD was considered hepatic steatosis which could be diagnosed by ultrasound.The implications of the ultrasound results highlighted that higher physical activities supported maintaining better metabolic health and also supported lowering the circumference of the waist and insulin resistance.Thus,from the use of the ultrasound process with the neural network model,the researchers have effectively suggested that proper incorporation of physical activities could be incorporated into the management of NAFLD disease as well as the programs of prevention.

Pang et al. (2022) elaborated in a study that due to the increasing burden of obesity and related NAFLD global health organisations consider these global health crises.However,in this process, the role of circulating metabolomic bio-markers is known to be very little in order to establish an association with them.The researchers in this aspect targeted to evaluate the observational and generic associations of adiposity with the metabolic bio-markers and also targeted on evaluating the observational associations of incident NAFLD with metabolic bio-markers.In order to assist the same linear regression has been followed through the consideration of certain adjustments for multiple testing.Along with that Cox regression was utilized to determine the adjusted HRs for NAFLD related to bio-markers.Considering the findings the researchers have concluded that with NAFLD risk a certain range of metabolomic bio-markers is related.Further,it has also been ob-

served that bio-markers may form a pathway between NAFLD and adiposity.
In this process,Byra et al. (2018) targeted in their research paper to identify the implication and effectiveness of a neural network-based approach for NAFLD evaluation in the ultrasound process.For that purpose,the study utilized the Inception-ResNet-v2 deep convolutional neural network which was pre-trained on the dataset of ImageNet for supporting the extraction of high-level features in liver B-mode ultrasound image sequences. The proposed approach of the researchers has been observed to support the practitioners in automatically diagnosing the level of fat in the liver of a patient.Thus,it could be considered an effective approach consider and even opposite to other methods ultrasonography users also do not need to choose the region of interest.
Chou et al. (2021a) have focused their study to develop proper neural network-based models that could support analysing fatty liver and also classifying the level of severity with the implication of the images of ultrasound.The Formulated deep learning models of the researcher's effective performance in prediction making the most accurate level.However,was observed to be an expensive and non-invasive diagnostic method to be considered for treating and predicting fatty liver incidences.In this process,it is also essential to highlight that different discriminative abilities,such as mild steatosis,could create a significant impact on the applications at the clinical level of the fatty liver.However,the researchers also identified that it needed to overcome motion artefacts, machine-dependent variation,hospital-dependent regional bias and other factors as well.On the other hand,Thongchattu et al. (2019) aimed in their study to identify whether the implication of the backpropagation artificial neural network model could be formulated to predict NAFLD in an accurate manner.The higher level of accuracy, in this process,i.e.,96.34% with a sensitivity of 93.75% highlighted that proper implication of BP-ANN could be helpful for the practitioners to predict NAFLD and undertake proper management to reduce the adverse impact.Apart from that,Lee et al. (2021) proper application of AI and neural network model could be implemented to diagnose the NAFLD and deliver a proper means to develop suitable diagnosis methods as well.

6.4 Utilization of Machine Learning Models in NAFLD predictions

From the study by Ji et al. (2022)NAFLD is identified as a crucial health problem that is affecting people throughout the world and this disease is also lacking efficient and appropriate medical treatment as well.Considering that the researchers aimed to formulate and value the models of machine learning that could be utilised for accurate screening of a large number of people.In this process,it utilised absolute shrinkage and selection operator,commonly known as LASSO,for section and following that 4 machine learning algorithms were also implemented for building the NAFLD screening model.Based on the findings it could be identified that XGBoost delivered the best performance with an accuracy of 0.880 and precision of 0.801.It also indicated that ML classifiers could support the medical agencies or practitioners to make early identification and classification of NAFLD,and further,the degree of covariate's importance could be helpful in preventing and treating NAFLD.
In another study,Nam et al. (2022) stated that healthcare practitioners are currently integrating different quantitative and qualitative information from different sources of data for making appropriate diagnoses and recommending treatment.Even the advancements in AI and the deep learning process have supported the extraction of relevant information

from diverse and complex clinical datasets as well.Considering that,the researchers targeted to summarise the implication of AI in hepatology while focusing on histopathology and radiology data.

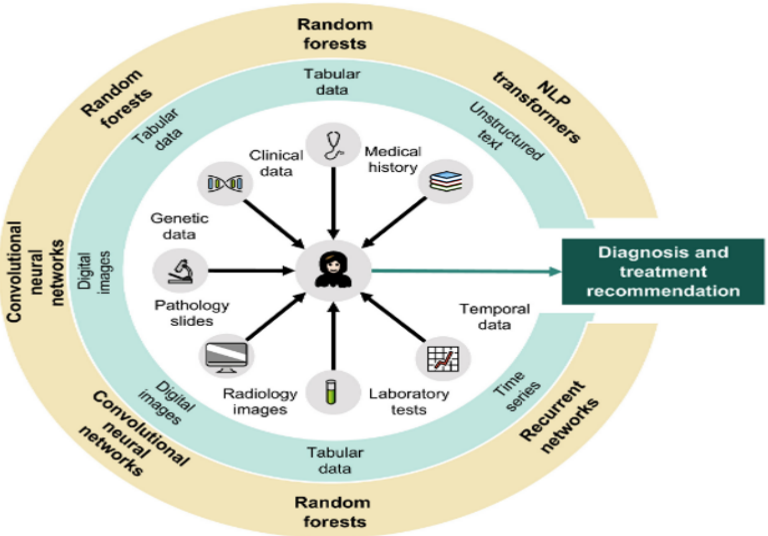

Figure 1: Data types in hepatology and multimodal learning

[1] Depending on the above figure(Figure 1)the researchers highlighted that the inner area of the image highlighted the routinely considered data that could be generally considered for clinical decision-making in hepatology.On the other hand, the circle coloured in blue shows different types of digital data to be considered whereas the yellow circle highlights the suitable methods of machine learning that could be used in the process of data analysis. Chou et al. (2021b) elaborated in their study that the presence of significant liver fibrosis Could be a crucial factor in the occurrence of NAFLD.The researchers in this study targeted to formulate a novel machine learning algorithm for predicting the severity of fibrosis in NAFLD.Apart from that,it is also considered to compare it with the widely used non-invasive fibrosis biomarkers as well.In this regard,considering the findings of the training cohort,it was observed that the variables chosen by the LASSO algorithm were BMI,collagen type IV,pro-collagen type III and others.It showed that the accuracy of diagnosis performed based on MLA delivered the highest values of the area in the case of the received operator characteristic curve.Even in the case of the validation cohort MLA provided the highest AUROC value i.e. 0.893,95% CI 0.864-0.901.Considering these findings the researchers concluded that the chosen MLA algorithm has successfully provided excellent performance in diagnostic that could predict fibrosis in the targeted patients with proper consideration of biopsy-confirmed NAFLD.
Targeted to evaluate the effectiveness of the ML model for predicting fatty liver disease that may support the practitioners in identifying high-risk patients and developing Wu et al. (2019)a proper diagnosis along with preventing and managing NAFLD.In this process,the researchers utilize different classification models such as artificial neural networks,random forest, logistic regression and Naive Bayes.The results showed that the accuracy level was the highest for the random forest with 87.48% whereas at 76.96% logistic regression was the lowest performing model.Thus,it indicates that among the chosen

[1]Source of Figure 1:Nam et al. (2022)

models random forest delivered the most accurate results for predicting the disease of fatty liver.Thus it could be concluded that the implication of this random forest model in the clinical setup could deliver the physicians with appropriate means to identify fatty liver patients and based on which proper prevention services along with surveillance,early treatment and management could be delivered.
Apart from that, Liu et al. (2021) elaborated in a study that NAFLD is a key or crucial public health challenge and it can act as a causing factor of morbidity and mortality throughout the world. In this process,it has been observed that early identification could be effective for developing a proper disease intervention plan as well.For that purpose,this study targeted on exploring the implication of machine learning tools at the time of predicting NAFLD.In the evaluation process,the researchers implemented different biochemical and clinical factors and algorithms of machine learning were also considered for developing and validating seven predictive models as well.Focusing on the outcomes it could be stated that the implication of the XGBoost model provided the best performance in predicting the ability for diagnosing NAFLD.Apart from that,it was also observed that the tools of machine learning could deliver higher benefits at the time of screening NAFLD.

6.5 Literature Gap

Based on the above literature or previous papers it could be identified that no previous study focused on using computed tomography scans along with ultrasonography focusing on neural networks and deep learning.Thus,consideration of these aspects in a single study would be highly effective to deliver a new dimension in making predictions of NAFLD stages as well.Further,it would be highly beneficial to develop a complex understanding of the focused area of research and provide a proper means of diagnosing NAFLD to the practitioners at different stages of the same.

6.6 Summary

This section has discussed previous studies and research papers that could help to develop a proper understanding of the present usage of ultrasonography and computed tomography scans in the process of predicting NAFLD at different stages.These studies have also shown that there is a large scope available to develop a proper predicting strategy using technology and data which can support the practitioners to identify or predict the likelihood of occurrence of NAFLD and deliver proper services as well.Hence, this study could deliver a higher value to the practitioners as well as to the patients who are affected by NAFLD.

7 Methodology

This section discusses the methodology followed in the research.The steps that are undertaken in the methodology are depicted in the figure below.The study considers the hematological data for the patients.The data corresponds to the hematological features associated with different stages of liver disease.The blocks or modules involved in the study are depicted in figure(Figure¬2) and are discussed in detail below.

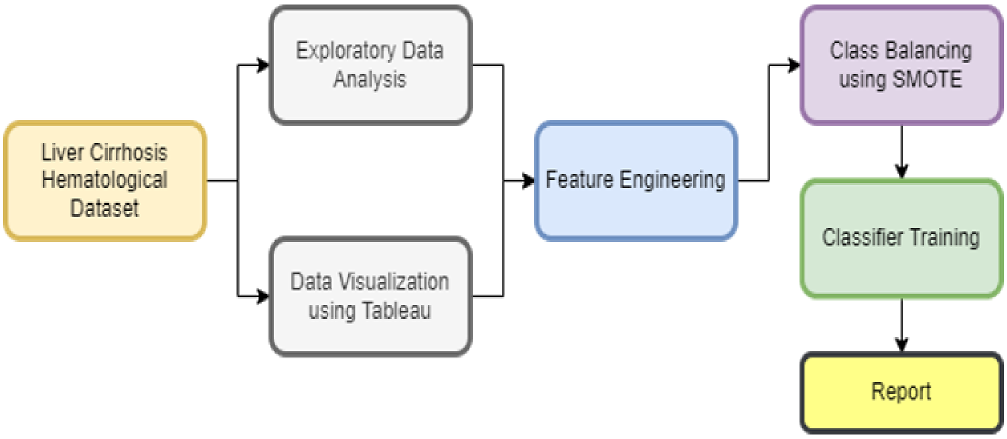

Figure 2: Research Process

The figure(Figure 2) above depicts the sub-processes that are performed to achieve the goals of the study. First module of the study is finding a proper dataset that can be used in the study.After the dataset is found,it is thoroughly studies using data visualization techniques such as Exploratory Data Analysis (EDA).Once the dataset is studied,important features are identified to construct a feature vector.As the dataset contains imbalanced classes,synthetic features have to be generated.This is done using class balancing techniques such as SMOTE.Once the class balancing is performed,the feature vector can be used to train the models with part of the data and testing them over the remaining part.A classification report is generated using the results obtained after classification.

7.1 Dataset

The dataset that has been identified for the study is created during the Mayo Clinic trial of Preliminary Biliary Cirrhosis (PBC) of the Liver conducted between 1974 and 1984 .The dataset contains information about 424 PBC patients that has a total of 20 attributes.The attributes present in the dataset are listed in the table(Table 1) below.
[2]

7.2 Data Visualization

Data visualization is an important step in any research as it helps the researcher identify important features from the dataset.It makes use of graphs and plots to help the researcher infer significant aspects of the data.It also gives the distribution of classes in the dataset which can help the analyst to implement class balancing techniques in the study.It also helps identify the correlation between the features such that the most prominent features of the dataset can be obtained.This study implements data visualization using Tableau software.Tableau is a powerful Business Intelligence software used across industries for analyzing data.Data visualization helps identify redundant features in the dataset.Removing these features helps achieve better reliability for the classification.

[2]https://www.mayo.edu/research/documents/pbchtml/doc-10027635

Table 1: Dataset Attributes

Sr.No	Attribute	Attribute Information	Values
1	ID	Unique Identifier	Number
2	N_Days	Days after the registration	Number
3	Status	Status of the patient (Censored or Dead)	C/CL/D
4	Drug	Type of Drug Patient is on	D-Penicillamine or Placebo
5	Age	Age of the patient in days	Number
6	Sex	Sex of the patient	String
7	Ascites	Denotes the presence of Ascites	Yes/No
8	Hepatomegaly	Denotes the presence of Hepatomegaly	Yes/No
9	Spiders	Denotes the presence of Spiders	Yes/No
10	Edema	Denotes the presence of edema with or without diuretic therapy	Y/S/N
11	Bilirubin	Serum Bilirubin in mg/dl	Number
12	Cholesterol	Serum Cholesterol in mg/dl	Number
13	Albumin	Albumin in gm/dl	Number
14	Copper	Urine Copper in ug/day	Number
15	Alk_Phos	Alkaline Phosphatase in U/L	Number
16	SGOT	SGOT value in U/ml	Number
17	Triglycerides	Triglycerides in mg/dl	Number
18	Platelets	Blood platelets per cubic ml/1000	Number
19	Prothrombin	Prothrombin time in seconds	Number
20	Stage	Histologic stage of the disease	1/2/3/4

7.3 Feature Engineering

The models used in the study do not explicitly have the ability to perform operations on non-numerical data.Hence the features that are selected from the dataset need to be pre-processed before processing them.There are some features in the dataset that contain non-numerical values.These features are status,sex and edema.Values of these features are then converted to numerical form using the technique called label encoding.Label encoding is the process of identifying unique values in the feature and replacing them using a number.This makes the data machine or model readable and easy to process.

7.4 SMOTE-based class balancing

From the dataset,it can be observed that the class samples in the dataset are not balanced.For a reliable classification of the data,balanced classes are required which means the number of samples corresponding to each of the classes must be the same.To balance

such data different class balancing techniques can be used.One of them is Synthetic Minority Oversampling Technique (SMOTE).As the name suggests,this technique oversamples the class samples in minority by synthetically creating new samples for the minority classes.All the samples that are less in number or in minority are oversampled to have the same instances as that of the Majority class.
The data augmentation or generation in SMOTE is done as follows:
1. Draw a random sample from the minority class.
2. Identify k nearest neighbors to the sample drawn.
3. Identify a vector between the sample and one of the k-neighbors.
4. Multiply the vector by a number between 0 and 1.
5. Add the value to the current sample to get the synthetic data point.

7.4.1 Recurrent Neural Network (RNN)

Neural networks are machine learning models that try to mimic the ability of the human brain to identify patterns in the data.They are characterized by nodes that are similar to neurons in the brain.These nodes are connected through connections known as synapses.The synapses are given a value denoting their importance. These values are known as synaptic weights.Activation of the neurons or nodes is defined using an activation function that relates the weighted sum of outputs of the nodes to a threshold.Values greater than this threshold are assigned to the class else not.The figure(Figure 3)below depicts a generalized architecture of the neural network.The neurons displayed in blue are input neurons and the layer consisting of these neurons is known as input layer.Neurons in yellow depict the hidden neurons.Hidden neurons are not connected to the input or the output directly but are the most essential part of a neural network.Their connections to input and output neurons are responsible for the model training.Purple neurons in the figure are called output neurons and are supplied by an activation function to output the results.

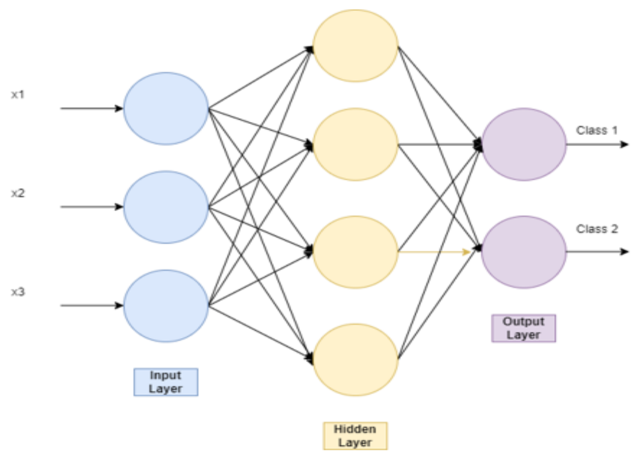

Figure 3: Neural Network Architecture

[3] Recurrent neural networks are a class of neural networks that have the ability to process sequential data.Recurrent neural networks are characterized by the presence of a

[3]Figure 3:Created using www.diargrams.net

memory cell.Memory cell helps retain information that was acquired from previous processing.This information is stored in the synaptic weights between the nodes.These nodes are called hidden nodes.These nodes are present between the input and the output layers of the model.A layer is nothing but the collection of nodes/neurons.A simple conventional recurrent neural network consists of a single hidden layer.

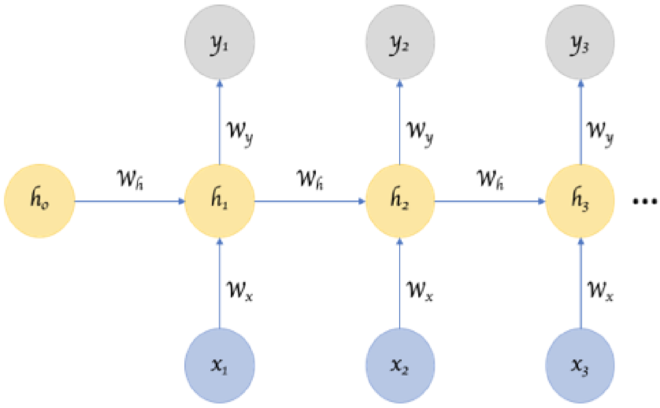

Figure 4: Recurrent Neural Network Architecture

[4] Figure(Figure 4) above depicts the architecture of an RNN.Neurons denoted with x are input neurons,those denoted with h are hidden neurons while those represented by y are output neurons.Figure above shows that the hidden neurons in current layer are supplied with the hidden neuron of previous state.Weights representing their connections are given by Wh.Value of Wh is updated after each epoch.Wh hence is responsible for storing the information of the previous state of the RNN.

7.4.2 Deep Recurrent Neural Network (DRNN)

A deep recurrent neural network is a more sophisticated recurrent neural network. It has greater than 1 number of hidden layers.Deep neural networks are found to be more accurate compared to their simple versions as they are able to store more information and the biases are reduced due to the large number of hidden layers.

7.4.3 Support Vector Machines

Support vector machines are probabilistic models of classification.Generally developed for binary classification i.e.the classification into two classes,SVM can be used for multiclass classification using strategies such as One vs One and One vs All.The aim of the SVM is to identify a classification boundary that reliably classify the data.This decision boundary is known as hyperplane.

[4]Figure 4:Created using www.diargrams.net

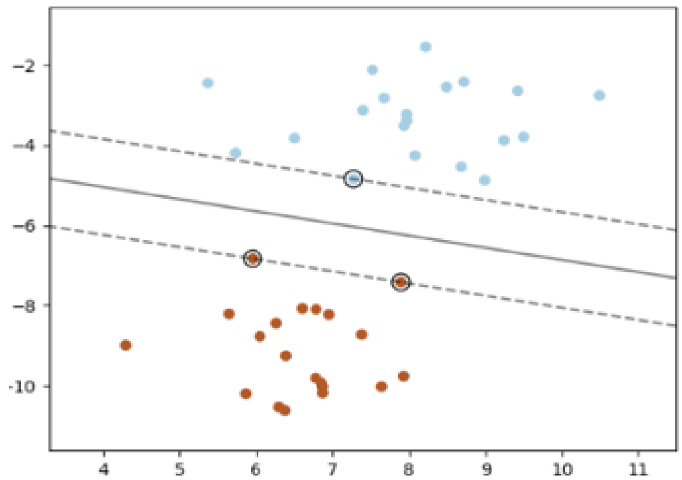

Figure 5: SVM Hyperplane

[5] Figure(Figure 5)above displays the hyperplane separating the classes represented by colours red and blue.The features on the dashed line in the figure are known as supports.SVM tries to maximize the distance between the supports in order to achieve the perfect classification.SVM generally are linear classifiers but they can be improved to classify non-linear data using a technique called kernel trick.In kernel trick,the data to be classified is converted to a higher dimension making it easy to define a classification boundary.

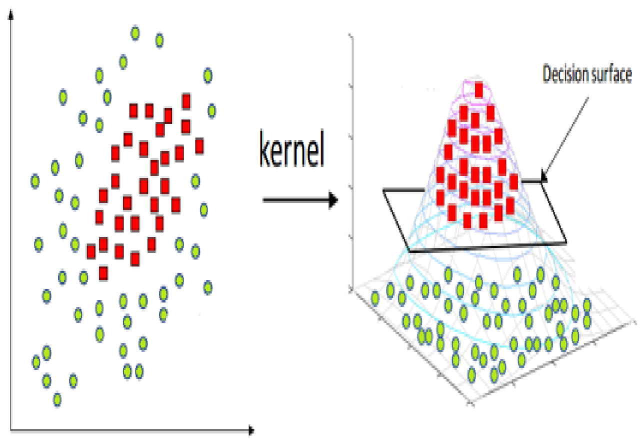

Figure 6: Kernel Trick

[6] Figure(Figure 6)above depicts the application of kernel in SVM.Observe that the data on the left in figure 6 is not linearly separable.To separate the classes, the feature space which is in 2D is transformed into a 3D feature space as seen in the figure on the right.This is done using a kernel which can be a Gaussian kernel (shown in figure),polynomial kernel or Radial Basis Function(RBF).Note that the hyperplane for a 3D feature space becomes a 2D plane.

[5]Figure 5:www.scikit-learn.org
[6]Figure 6:www.mdpi.com

7.4.4 Random Forest

Random forest is an ensemble based learning method in which a forest is a collection of decision trees.These trees generate relationships between feature samples in order to classify the samples into classes.The random forest considers the class with highest occurrences across the decision trees to be the output class this is depicted in figure(Figure 7).As the tree generation is sequential in nature,these classifiers are considered to be good at classification of sequential data.
Figure below shows that decision trees act on sub-samples(N).Results of all these trees are classes representing the samples.The final prediction is selected based on the voting or averaging of these outputs.

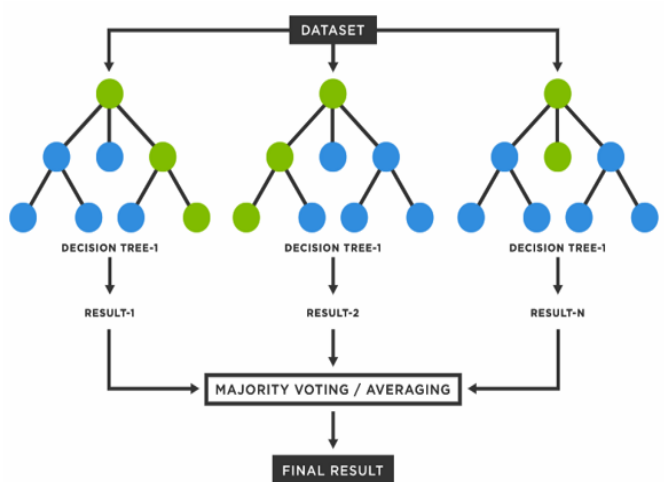

Figure 7: Random Forest Algorithm

[7]

7.5 Evaluation

The models that are developed in the study can be evaluated for their reliability using distinct evaluation metrics.These metrics are listed below.
1. **Accuracy -**Ability to correctly classify the classes.
2. **Precision -**Gives the fraction of positives amongst all the positives.
3. **Recall -**True positives amongst all the predictions.
4. **F1-score -** Harmonic mean of the precision and recall.

7.6 Architecture of Model

This section of the thesis explains the architecture of the models used in the study.

[7]Figure 7:www.tibco.com

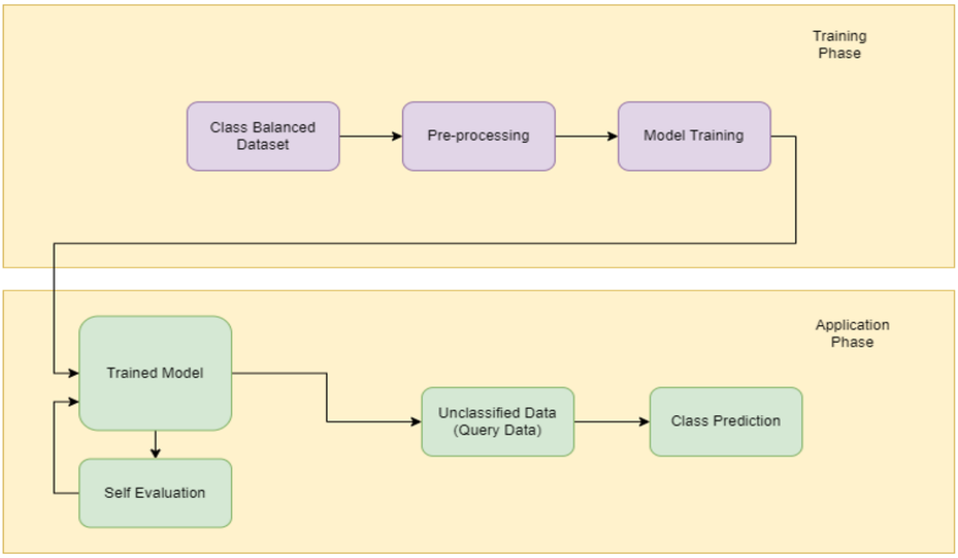

Figure 8: Classification Architecture

[8] Figure(Figure 8)above depicts the classification architecture. From the figure,it can be seen that the dataset after the SMOTE is split into two subsets viz.are training dataset and the testing dataset in a proportion that is considered to be sufficient for the model.The model for classification is trained on the training dataset.Model identifies the pattern in the dataset and learn from it.The trained model is then applied on the testing data.The testing data acts an unknown data for the model.Model then assigns a class that it seems fit to each sample in the testing dataset.This process is known as classification.

7.6.1 Comparison of Models with Each Other

Table 2: Comparison of Machine Learning Models

Model	Class	Hyper parameters Tuning
Recurrent Neural Network	Neural Network	Self-Tuned
Deep Neural Network	Deep Neural Network	Self-Tuned
Support Vector Machines	Probabilistic Classifier	Required Specifically
Random Forest	Ensemble Learning	Required Specifically

Models that have been used in the study are compared in the table(Table 2)above.The recurrent neural networks and the Deep Recurrent Neural Networks belong to the class of

[8]Figure 8:Created using www.diagrams.net

neural networks that are discussed in sections 7.4.1(Recurrent Neural Network (RNN)), and 7.4.2(Deep Recurrent Neural Network (DRNN)).These neural networks do not require any hyper-parameter tuning as they learn and adjust their weights from the data itself.SVM which is a probabilistic classifier requires selection of tuned hyper-parameters viz.C and Gamma (in case of RBF kernel). Where C is the cost parameter,and gamma gives the slope of the RBF kernel. For RF classifier,the hyper-parameter that needs to be selected is the number of decision trees that are present in the forest.

7.6.2 Comparison of Model with the Latest Research Papers Model

Table 3: Comparison of Models used Across Studies

Sr.No	Author	Classifier Models	Evaluation
1	Alkhatib A J (2022)	Artificial Neural Network	Accuracy= 79.70%
2	Servenstany et al (2022)	Ensemble of Classifiers based on SVM, Random Forest, Gradient Boosting Classifier, Logistic Regression and Neural Networks	AUROC= 100%
3	Patnaik et al (2021)	Logistic Regression,Random Forest,Support Vector Regression,Extra Tree Regression	RMSE= 0.26,0.53,0.65,0.55
4	Nam et al (2022)	Convolutional Neural Network	AUC= 0.85
5	Ji et al (2022)	5. Ji et al (2022) Logistic Regression,Random Forest Regression,XGBoost,Naive Bayes	Accuracy= 0.77,0.86,0.88,0.71
6	Perrakis et al (2019)	Logistic Regression,Decision Trees,Random Forest,SVM,XGBoost	Sensitivity= 0.72,0.7,0.69,0.73,0.72

8 Results

This section elaborates the outcome of the research through the results obtained via experimentation.The aim of this research has been to identify the possibility of detecting the liver disease progression beforehand using haematological data available in the dataset.This has been done using four distinct models of machine learning viz.Recurrent Neural Network,Deep Recurrent Neural Network,Support Vector Machines,and Random Forest.

8.1 Data Visualization using Tableau

Figure(Figure 9)below displays the dashboard 1 of the Tableau in which the number of days are compared with the status of the patient.Blue region in the figure represents the status C,red region indicate the status D,orange region indicate the status CL.From figure it can be observed the number of days for status C is maximum.The second worksheet of the dashboard compares the number of days for the Drugs.The worksheet shows that D-penicillamine administered patients show maximum number of Days.

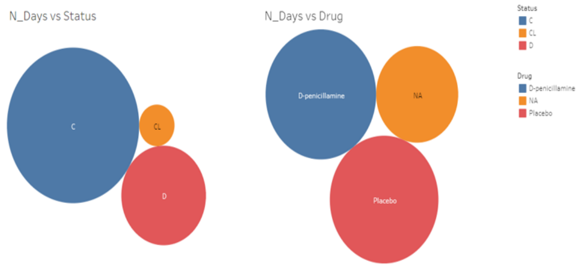

Figure 9: Dashboard 1

The comparison of age with the status is depicted in the first worksheet of Dashboard 2 displayed in figure(Figure 10).The figure consists of pie-charts to compare status with age and stage.Worksheet 1 of the dashboard implies that the age is maximum for the status C of the disease followed by D and CL.Second worksheet in the dashboard compares status and stage in which the patients with status C are the most in number.

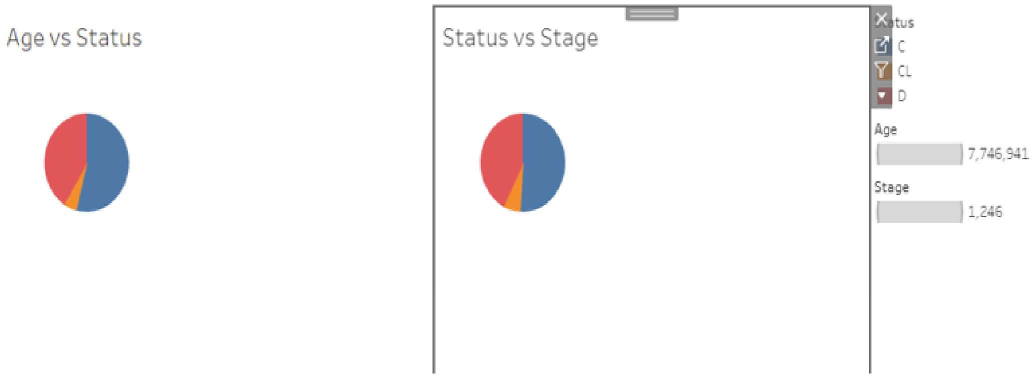

Figure 10: Dashboard 2

Figure(Figure 11)below depicts the dashboard 3 wherein the comparison of sex with stage,Prothrombin,Platelets,Albumin,Bilirubin is done. First worksheet in the dashboard compares the sex with stage and here female has maximum stage as compare to male,the second worksheet compares the sex with Prothrombin and here female has maximum prothrombin than male,in the third worksheet here female has the maximum platelets than male,in the fourth worksheet female has maximum albumin than male and in the last worksheet here female has the maximum Bilirubin than male.

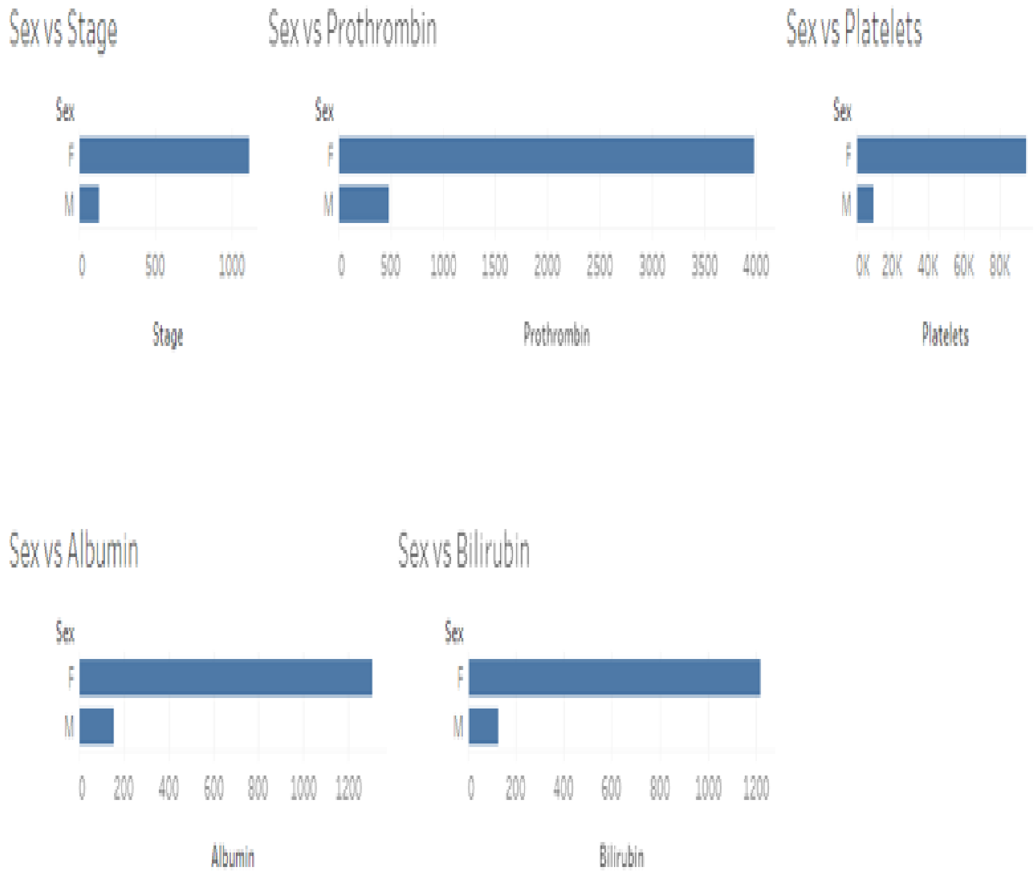

Figure 11: Dashboard 3

Dashboard 4 of the data visualization in Tableau is depicted in the figure(Figure 12) below.It consists of two worksheets.First worksheet compares N_Days attribute with Hepatomegaly. From the worksheet it can be seen that the N_days is maximum for patients with no hepatomegaly. The second worksheet compares cholesterol level with N_days with the sex attribute.The worksheet indicates that female with cholesterol are more in number.

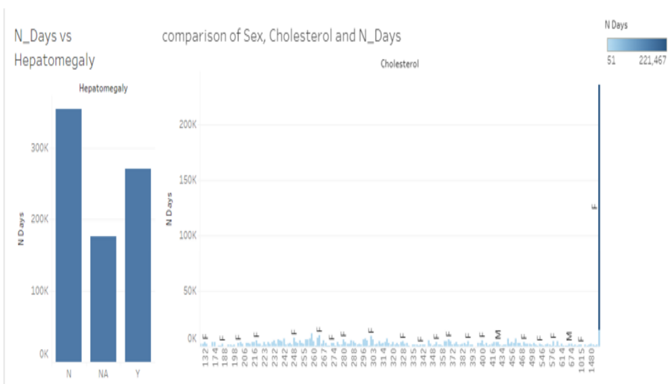

Figure 12: Dashboard 4

Dashboard 5 of the Tableau represents comparison of Stage with Edema and Hepatomegaly in worksheet 1 and 2 respectively in figure(Figure 13). The dashboard shows that the patients with higher histologic stage of the disease show presence of the edema.Second worksheet show higher stage of the disease show hepatomegaly.

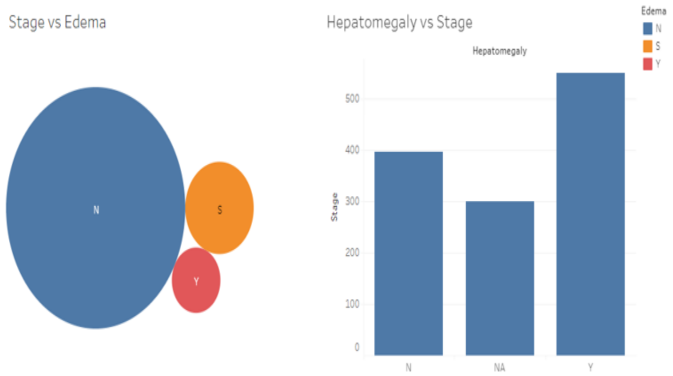

Figure 13: Dashboard 5

Figure(Figure 14)displays the dashboard 6 consisting of the worksheet showing patients health data using bubble plot.The dark blue bubbles indicate patients with higher stage and pale blue bubbles indicate lower stage in patients.Second worksheet indicate higher stage for placebo compared to those on D-penicillamine.

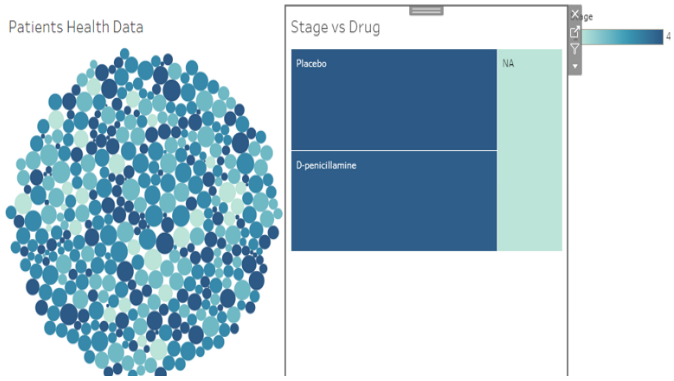

Figure 14: Dashboard 6

Dashboard 7 shown in (Figure 15)depicts the relationships between attributes of the dataset.Worksheet 1 of the dashboard relates SGOT,status and age with each other using bubble plot.(Figure 15)indicates that the patients with status C and D show higher values of SGOT compared to those of status CL.Second worksheet relates spiders,triglycerides and stage.It indicates that spiders,triglycerides and the stage are not correlated.

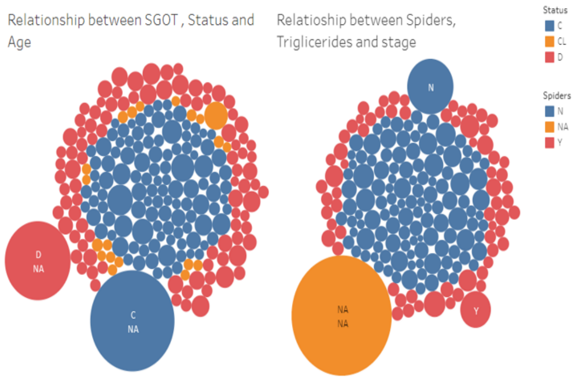

Figure 15: Dashboard 7

Figure(Figure 16)below shows the dashboard 8 consists of 2 worksheets of which the first worksheet compares the drugs attribute with platelets.It indicates that the drugs has higher platelets.Second worksheet shows that the placebo drug shows maximum stage.

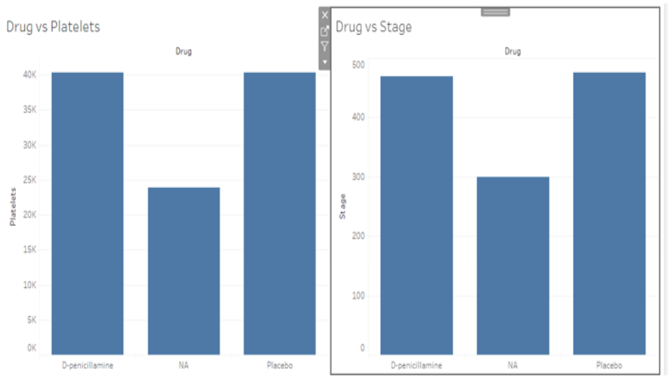

Figure 16: Dashboard 8

Dashboard 9 of the visualization is depicted in figure(Figure 17)below.Worksheets in the dashboard depicts pie-plots comparing N_days vs Drugs and Status vs Prothrombin.The blue region in the worksheet 1 represents D-penicillamine while the red region indicates placebo.Blue region in worksheet 2 indicates status C,red region indicates status D and orange region indicates status CL for the patients.

Figure 17: Dashboard 9

8.2 Machine Learning Modeling Results

Following table(Table 4)depicts the results obtained for the machine learning algorithms that have been implemented and studied in the research.Accuracy values for the implemented models are depicted in table 4 below. From the table,it can be seen that the

Table 4: Accuracy Table for Models

Machine Learning Model	**Accuracy**	**Balanced Accuracy**
Recurrent Neural Network	62.5	73.7
Deep Neural Network	**73.3**	**96.7**
Support Vector Machines	57.5	84.2
Random Forest	68.3	94.2

highest value of accuracy has been obtained for the Deep Recurrent Neural Network.The models can be evaluated further using metrics of precision,recall and f1-score.The values of these metrics are as given in the tables below.Confusion matrix is another method of visually determining the model performance.Confusion matrices for the implemented models are depicted in figures below. Table(Table 5)below enlists the metrics for recurrent neural networks.From the table it can be seen that for recurrent neural network,the highest precision,recall and F1-score is obtained for the Class 1 with value of 0.78 ,0.89 and 0.83 respectively.Confusion matrix denotes the possibility of misclassification for a model.Figure below is the confusion matrix for the recurrent neural network.The accuracy of the model can also be obtained from the matrix by calculating correctly classified and misclassified classes.

Table 5: Performance Metrics for RNN

Recurrent Neural Network			
Class/Stage	**Precision**	**Recall**	**F-1 Score**
1	**0.78**	**0.89**	**0.83**
2	0.50	0.38	0.43
3	0.45	0.56	0.50
4	0.76	0.68	0.72

Figure 18: Confusion Matrix for RNN

Table(Table 6)below enlists the metrics for deep recurrent neural network.The table depicts that the highest value of precision and f1-score are obtained for the Class 1 whereas the highest values of recall score are obtained for the Class 2.These metrics in overall denotes the reproducibility of the results. Figure(Figure 19)below,depicts the confusion matrix for the deep recurrent neural network model. Visually, from the confusion matrix,it can be identified that the model does not perform well in the classification of Class 3 and Class 4 of the data or it can be said that the model performs better for identification of Classes 1 and 2.

Table 6: Performance Metrics for DRNN

Deep Recurrent Neural Network			
Class/Stage	Precision	Recall	F-1 Score
1	**0.95**	0.75	**0.84**
2	0.62	**0.77**	0.69
3	0.58	0.72	0.64
4	0.83	0.71	0.76

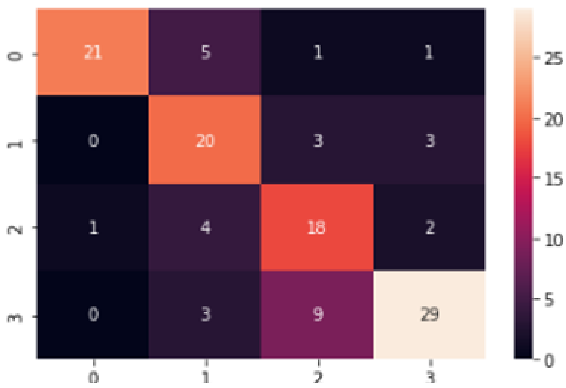

Figure 19: Confusion Matrix for DRNN

Table(Table 7)below depicts the performance metrics for SVM.The highest value of precision is obtained for Class 1 data with a value of 0.48.The highest values of recall and F1-score are obtained for Class 1 with values of 0.88 and 0.58 respectively. The confusion

Table 7: Performance Metrics for SVM

Support Vector Machines			
Class/Stage	Precision	Recall	F-1 Score
1	0.60	**0.89**	**0.71**
2	0.50	0.27	0.35
3	0.41	0.48	0.44
4	**0.71**	0.61	0.66

matrix for the SVM is shown below.SVM shows high possibilities of misclassification for Class 2 and Class 3 data.

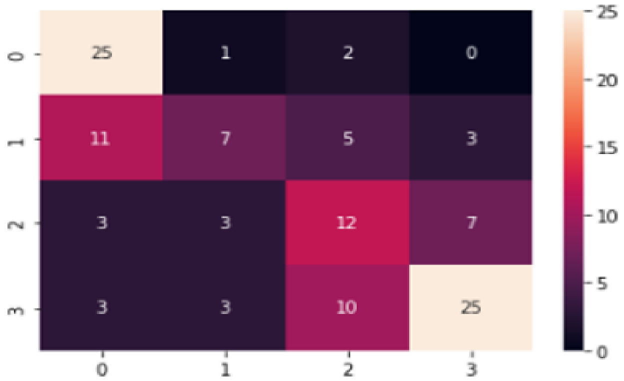

Figure 20: Confusion Matrix for SVM

Evaluation metrics for Random Forest model are enlisted in the table below.It can be seen from the table that RF has been able to reliably classify Class 1 and 4 but failed to perform for other Classes.This is also visible in the confusion matrix depicted in figure 21 below respectively.

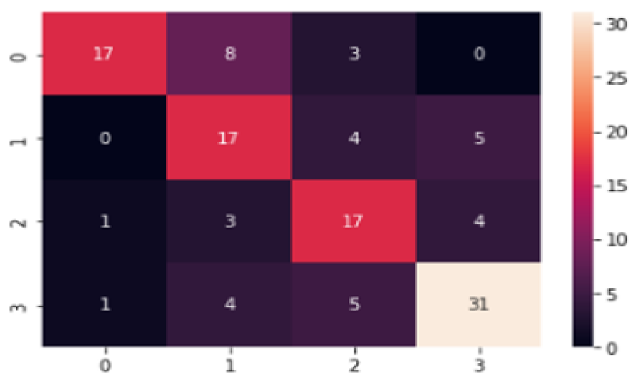

Figure 21: Confusion Matrix for Random Forest

Table 8: Performance Metrics for Random Forest

Random Forest			
Class/Stage	Precision	Recall	F-1 Score
1	**0.89**	0.61	0.72
2	0.53	0.65	0.59
3	0.59	0.68	0.63
4	0.78	**0.76**	**0.77**

9 Conclusion

Liver cirrhosis is mostly associated with chronic alcoholism but NAFLD has a possibility that it can be progressed into more dangerous disease known as Liver Cirrhosis.Hematological tests such as the Liver Function Test (LFT) are important biomarkers to identify affected metabolism in the organ.Specialists make use of such tests along with modern imaging technology to identify the progression of the NAFLD.
This study considered hematological features for implementing an assistive system that will help the specialist to confirm the prognosis.The study implemented four distinct models of machine learning for predictions viz.Recurrent Neural Network,Deep Recurrent Neural Network,Support Vector Machines, and Random Forest.These implemented models have been studied and evaluated based on evaluation metrics to identify their performance.
The recurrent nature of the recurrent neural networks helps in the classification of sequential data.This phenomenon is evident from the results obtained.The deep recurrent neural network model performed better than other models achieving the highest accuracy of 73% and the balanced accuracy score of 96.7%.The deep nature of deep recurrent neural networks,which implies high number of hidden layers helped the model perform better than the conventional RNN.
Random Forest algorithm have been another set of machine learning models that perform well on sequential data.The random forest being an ensemble-based learning model identifies the decision tree with the highest accuracy as the classifier.This ensemble nature of the RF helped achieve better performance than SVM and conventional RNN.SVM classifier used in the study performed the worst among the classifiers with a mere accuracy of 57%.
The balanced accuracy score is generated by using the sensitivity and specificity respectively particularly focusing on this research.The values of these score keep changing from time to time.
From the study,it can be concluded that the detection of the progression of liver disease is a task involving very high difficulty.With the highest balanced accuracy of 96.7%,the models cannot be utilized for automated detection of the progression.However,the accuracy can be considered reliable for assisting a specialist in detecting the progression.

10 Future Work

The accuracy of the models can be improved using a larger dataset while implementing deep learning frameworks.Deep learning models such as Gated Recurrent Units and Convolutional Neural Networks have been found to be very powerful at classification.These models can be continuously trained with newer data to improve their accuracies.As the dataset available for the study is small,data simulation can be performed to collect new data.Consented study of the patient's data via clinics can be used to enlarge the dataset,as doing this will improve the reliability of the models that have been developed.

References

Alkhatib, A. J. (2022). Relative contribution of liver disease risk factors in the prediction of liver diseases using artificial intelligence, *Adv. Obes. Weight Manag. Control* **12**(1): 1–4.

Byra, M., Styczynski, G., Szmigielski, C., Kalinowski, P., Michałowski, Ł., Paluszkiewicz, R., Ziarkiewicz-Wróblewska, B., Zieniewicz, K., Sobieraj, P. and Nowicki, A. (2018). Transfer learning with deep convolutional neural network for liver steatosis assessment in ultrasound images, *International journal of computer assisted radiology and surgery* **13**(12): 1895–1903.

Castera, L. (2018). Diagnosis of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis: non-invasive tests are enough, *Liver International* **38**: 67–70.

Chen, H., Wu, L., Dou, Q., Qin, J., Li, S., Cheng, J.-Z., Ni, D. and Heng, P.-A. (2017). Ultrasound standard plane detection using a composite neural network framework, *IEEE transactions on cybernetics* **47**(6): 1576–1586.

Choi, E., Schuetz, A., Stewart, W. F. and Sun, J. (2017). Using recurrent neural network models for early detection of heart failure onset, *Journal of the American Medical Informatics Association* **24**(2): 361–370.

Chou, T.-H., Yeh, H.-J., Chang, C.-C., Tang, J.-H., Kao, W.-Y., Su, I.-C., Li, C.-H., Chang, W.-H., Huang, C.-K., Sufriyana, H. et al. (2021a). Deep learning for abdominal ultrasound: A computer-aided diagnostic system for the severity of fatty liver, *Journal of the Chinese Medical Association* **84**(9): 842–850.

Chou, T.-H., Yeh, H.-J., Chang, C.-C., Tang, J.-H., Kao, W.-Y., Su, I.-C., Li, C.-H., Chang, W.-H., Huang, C.-K., Sufriyana, H. et al. (2021b). Deep learning for abdominal ultrasound: A computer-aided diagnostic system for the severity of fatty liver, *Journal of the Chinese Medical Association* **84**(9): 842–850.

Ji, W., Xue, M., Zhang, Y., Yao, H. and Wang, Y. (2022). A machine learning based framework to identify and classify non-alcoholic fatty liver disease in a large-scale population, *Frontiers in Public Health* **10**.

Lee, H. W., Sung, J. J. and Ahn, S. H. (2021). Artificial intelligence in liver disease, *Journal of Gastroenterology and Hepatology* **36**(3): 539–542.

Liu, Y.-X., Liu, X., Cen, C., Li, X., Liu, J.-M., Ming, Z.-Y., Yu, S.-F., Tang, X.-F., Zhou, L., Yu, J. et al. (2021). Comparison and development of advanced machine learning tools to predict nonalcoholic fatty liver disease: an extended study, *Hepatobiliary & Pancreatic Diseases International* **20**(5): 409–415.

Lupsor-Platon, M., Serban, T., Silion, A. I., Tirpe, G. R., Tirpe, A. and Florea, M. (2021). Performance of ultrasound techniques and the potential of artificial intelligence in the evaluation of hepatocellular carcinoma and non-alcoholic fatty liver disease, *Cancers* **13**(4): 790.

Nam, D., Chapiro, J., Paradis, V., Seraphin, T. P. and Kather, J. N. (2022). Artificial intelligence in liver diseases: improving diagnostics, prognostics and response prediction, *JHEP Reports* p. 100443.

Neuschwander-Tetri, B. A. (2017). Non-alcoholic fatty liver disease, *BMC medicine* **15**(1): 1–6.

Pang, Y., Kartsonaki, C., Lv, J., Millwood, I. Y., Fairhurst-Hunter, Z., Turnbull, I., Bragg, F., Hill, M. R., Yu, C., Guo, Y. et al. (2022). Adiposity, metabolomic biomarkers, and risk of nonalcoholic fatty liver disease: a case-cohort study, *The American journal of clinical nutrition* **115**(3): 799–810.

Sharma, D., Gotlieb, N., Farkouh, M. E., Patel, K., Xu, W. and Bhat, M. (2022). Machine learning approach to classify cardiovascular disease in patients with nonalcoholic fatty liver disease in the uk biobank cohort, *Journal of the American Heart Association* **11**(1): e022576.

Sorino, P., Campanella, A., Bonfiglio, C., Mirizzi, A., Franco, I., Bianco, A., Caruso, M. G., Misciagna, G., Aballay, L. R., Buongiorno, C. et al. (2021). Development and validation of a neural network for nafld diagnosis, *Scientific Reports* **11**(1): 1–13.

Tang, Z., Chen, Z., Bao, Y. and Li, H. (2019). Convolutional neural network-based data anomaly detection method using multiple information for structural health monitoring, *Structural Control and Health Monitoring* **26**(1): e2296.

Thongchattu, C., Buangam, K., Duangjai, A., Phisalprapa, P., Kositamongkol, C. and Saokaew, S. (2019). Artificial neural network to predict nonalcoholic fatty liver disease in metabolic syndrome patients., *Gut & Liver* **13**.

Van Kleef, L. A., Hofman, A., Voortman, T. and De Knegt, R. J. (2022). Objectively measured physical activity is inversely associated with nonalcoholic fatty liver disease: The rotterdam study, *The American journal of gastroenterology* **117**(2): 311.

Wu, C.-C., Yeh, W.-C., Hsu, W.-D., Islam, M. M., Nguyen, P. A. A., Poly, T. N., Wang, Y.-C., Yang, H.-C. and Li, Y.-C. J. (2019). Prediction of fatty liver disease using machine learning algorithms, *Computer methods and programs in biomedicine* **170**: 23–29.

Younossi, Z., Tacke, F., Arrese, M., Chander Sharma, B., Mostafa, I., Bugianesi, E., Wai-Sun Wong, V., Yilmaz, Y., George, J., Fan, J. et al. (2019). Global perspectives on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, *Hepatology* **69**(6): 2672–2682.